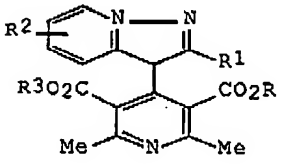
CHEMICAL ABSTRACTS RECORD FOR JP05025168

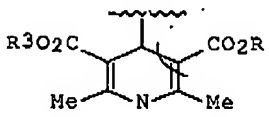
L2 ANSWER 1 OF 1 HCAPLUS COPYRIGHT 2002 ACS
AN 1993:560270 HCAPLUS
DN 119:160270
TI Preparation of 2,6-dimethyl-4-(pyrazolo[1,5-a]pyridin-3-yl)pyridine-3,5-dicarboxylic acid derivatives for enhancing susceptibility of anticancer agents against cancer cells
IN Iinuma, Fuchio
PA Kyorin Seiyaku Kk, Japan
SO Jpn. Kokai Tokkyo Koho, 8 pp.
CODEN: JKXXAF
DT Patent
LA Japanese
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI JP--05025168	A2	19930202	1991JP-0173980	19910715 <--

OS MARPAT 119:160270
GI



I



II

AB The title compds. [I; R, R3 = (cyclo)alkyl, aralkyl, alkoxyalkyl, ANR4R5; A = linear or branched alkylene; R4, R5 = H, alkyl, aralkyl, or NR4R5 forms 5- to 6-membered heterocyclyl optionally contg. other hetero atoms; R1 = linear or branched alkylene; R2 = H, halo, alkyl, alkoxy, NO2], which show reduced Ca antagonist activity and acute toxicity and enhances susceptibility of various cancer cells including multidrug-resistant cancer cells to anticancer agents, are prepd. by oxidn. of dihydropyridine derivs. (II; R1 = R1 - R3 = same as above). Thus, a soln. of 1.2 g II (R = R3 = Me, R1 = iso-Pr, R2 = H) in THF was treated with 0.41 g 60% NaH with stirring at room temp., thereto 2.64 g diiodoethane was added in small portions under ice-cooling, and the mixt. was stirred at 50.degree. for 6 h to give 80% I (R = R3 = Me, R1 = iso-Pr, R2 = H). A combination of I (R = Me, R1 = iso-Pr, R2 = H, R3 = PhCH2NMeCH2CH2) and adriamycin in vitro showed IC50 of 3.2 .times. 10-5 mM against mouse leukemia P388 cells vs. 3.5 .times. 10-4 mM for adriamycin alone and 2.8 .times. 10-5 mM for a combination of known II (R = Me, R1 = iso-Pr, R2 = H, R3 = PhCH2NMeCH2CH2) (AHC-52) and adriamycin.